ALBERTA HERITAGE FOUNDATION FOR MEDICAL RESEARCH

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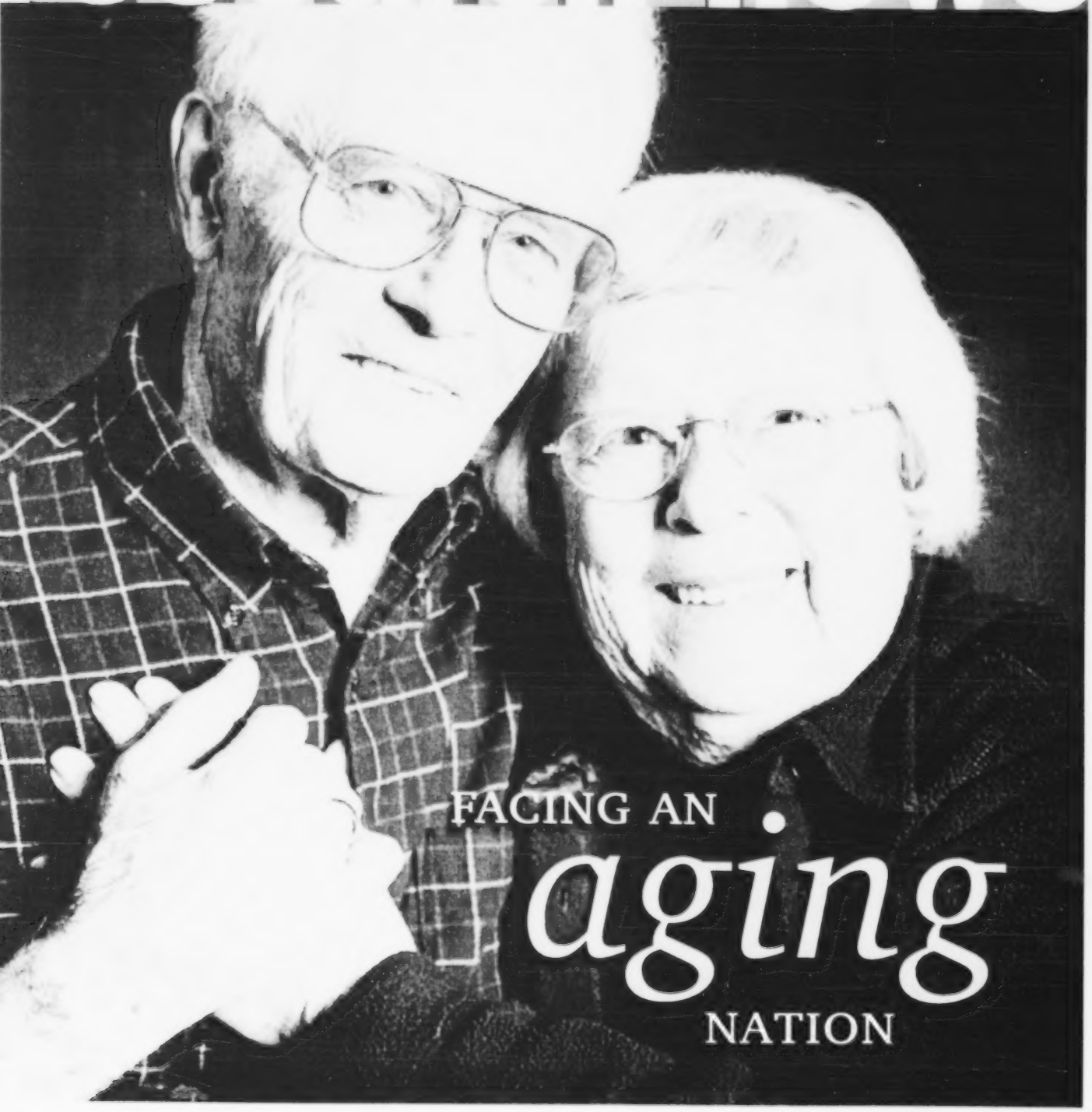
WINTER 2002



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research news

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AHFMR Mission

AHFMR supports a community of researchers who generate knowledge that improves the health and quality of life of Albertans and people throughout the world. AHFMR's long-term commitment is to fund basic, patient and health research based on international standards of excellence and carried out by new and established investigators and researchers in training.

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If a doctor asked you to participate in a clinical trial to test a new drug, what would you say? Could you be sure you would be told about all the risks? If it were discovered during the trial that the drug was harmful, would you be told?

Questions like this are occurring to many people these days. For Jocelyn Downie, Director of the Health Law Institute at Dalhousie University, they are part of a broader concern over the regulation of research in Canada. Downie outlined these issues in "Promises and Perils: Health Research in the New Millennium", the 2001 Honourable Mr. Justice Michael O'Byrne/AHFMR Lecture on Law, Medicine and Ethics.

"We are at a critical time, with many changes being made and a lot of posturing and turf establishment happening," she says. "I think that research participants and those affected by the results of research are imperilled right now.

"To raise concerns about research is not to question the legitimacy and value of research or the motives of many of the people involved in research. Research has taken us forward in remarkable ways in the past, and we are on the verge of many wonderful new developments. This goes beyond new treatments for diseases to new ways of thinking about prevention and health promotion, as well as policy development."

In Downie's view, the perils lie in the governance—or the lack of it—of research in Canada. "For example, there's little consistency in our approach to research," she says. "The various bits and pieces of provincial legislation that apply to research may not be consistent across the country.

"What are researchers and research ethics boards to do when our standard-setting documents don't set the same standard?"

For research conducted in institutions that receive funding from the Canadian Institutes of Health Research (CIHR), the Natural Sciences and Engineering Research Council (NSERC), and the Social Sciences and Humanities Research Council (SSHRC), there is the Tri-Council Policy Statement. It defines a common policy of ethical conduct for research involving human subjects.

But this policy is not comprehensive, says Downie. "It has huge gaps in it in terms of what it doesn't cover, such as community-based research and many aspects of genetic research.

"And because the Tri-Council Policy Statement only covers research done in institutions that receive funding from the three councils, this leaves an enormous amount of research unfettered. That's troubling, because you have a lot of private, industry-based research happening in doctors' offices and so on, and there's no control over it."

Another key issue for Downie is the lack of people who are adequately trained in research ethics. "Simply put, we don't have enough people with ethics training and expertise. We have a lot of well-meaning people who are serving on research ethics boards and who are knowledgeable about various aspects of research, but that isn't a substitute for ethics expertise, particularly at the level of policy-setting."

She notes that there is frequently a lack of understanding of what ethics expertise is. "An analogy is useful: say I have an interest in cardiology. I'm trained in law and philosophy, but off I go and spend a week or two at a university studying cardiology, getting all the basic principles, doing case studies. If I came back and announced to my local hospital that I should be practising cardiology, that would be absurd. And yet we do that with ethics.

"There's a level of distrust building around commercialization and conflicts of interest in research."

ABOVE: JOCELYN DOWNIE

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"Ethics is a long-established academic discipline. There are criteria by which you can measure ethics expertise, just as you do in other disciplines: where did the person study? What level of degree did they get? How much have they published? How many peer-reviewed research grants do they have? We could do this with ethics, and yet we often don't.

"The benign interpretation is that we don't understand ethics; the malign interpretation is that we don't want those people at the table because they're more trouble. People who have done just a bit of ethics, either coming from a health background or a legal background, may be less disturbing—in terms of both the kinds of questions they ask and the theoretical basis in which they will situate those questions. I'm most worried that we are seeing an eschewing of ethics expertise."

Another area of concern relates to institutional conflicts of interest, especially as universities and hospitals become increasingly dependent on industry funding. "Look at the amount of health research in Canada that's funded by the federal government (13%), compared to research funded by industry (the rest)," Downie says.

"This affects the research agenda, because there is pressure on researchers to do research that brings in money. There's little incentive, for example, to do research on diseases that affect a small number of people or a larger number of poor people. Industry funding shapes how research gets done and how research results get presented."

How to fix these problems? Downie proposes a body external to the funding councils that has the mandate to regulate all research in Canada, not limited to council-funded research. "I don't understand why every toaster in Canada needs to be checked, but not every research intervention," she says. "We have national standards for all kinds of things—why not research?

In Downie's view, the perils lie in the governance—or the lack of it—of research in Canada.

"This new organization would set standards and establish processes for ethics review. There would be a certain level of local ethics review and several national ethics review boards that would be responsible for things like multi-centre trials and novel or super-complex technologies. The exact structure needs to be figured out, and the complexity of the issues means there's no obvious, simple solution.

"But it's critical these discussions take place now. Researchers are quite keen, because they're so tired of having to deal with the incredible variations across the country. People are concerned about going to a doctor's office and being asked to be in a clinical trial. Am I sure they will tell me all the risks? Will they tell me if they discover something bad in the middle of the trial? Will researchers speak out publicly? There's a level of distrust building around commercialization and conflicts of interest in research.

"Research policies are being set. We need to speak up now—otherwise it could be too late."

Canadians know all too well the deadly nature of the *E. coli* bacteria. The *E. coli* strain 0157:H7 was responsible for the recent death of a two-year-old in New Brunswick and the outbreak that killed seven people in Walkerton, Ontario, in May 2000.

THE E. coli PUZZLE

Although most *E. coli* strains are harmless and live in the intestines of healthy humans and animals, this particular strain produces a powerful toxin and can cause severe illness.

But just how does an *E. coli* infection get started? This question intrigues Heritage Medical Scholar Dr. Rebekah DeVinney, an Assistant Professor in the Faculty of Medicine at the University of Calgary.

"If you ingest *E. coli* from food or water, it doesn't make you sick right away," she says. "The bacteria have to stick to your intestines. They have to establish residence. I'm interested in finding out exactly how they make this initial step."

Although Dr. DeVinney is in the early stages of her scientific career, she is already a pioneer in this area. While doing post-graduate work at the University of British Columbia in Dr. Brett Finlay's lab, she was part of the team that solved part of the puzzle of how these bacteria attach to the lining of the intestine. Most bacteria infect healthy cells by attaching themselves to proteins on the intestinal cell membrane. Certain *E. coli* strains do something quite different–they insert their own protein (known as Tir), which acts as a receptor to which they can then attach.

This groundbreaking work was done on an *E. coli* strain closely related to 0157:H7. In her own lab, Dr. DeVinney has turned her attention to 0157:H7 itself, which also uses Tir to attach to the membrane of intestinal cells. The insertion of Tir sets in motion a chain of events that rearranges cell structures and results in the formation of a "pedestal" that connects the bacteria to the intestinal cells.

"Formation of the pedestal is key to establishing infection," says Dr. DeVinney. "There's still a lot to learn about the role of Tir and other proteins in pedestal formation. This is a major focus of my research. If we could find out how pedestal formation is controlled, this information could be used by other teams to develop a treatment to block attachment of the bacteria and thus prevent colonization of the intestine by *E. coli*."

Dr. DeVinney's research involves painstaking laboratory work to develop *E. coli* strains with certain genes knocked out of them. They are then grown to see how the absence of each gene affects pedestal formation.

"These experiments are time-consuming, but I've always enjoyed lab work," says Dr. DeVinney, who worked as a lab technician before entering graduate school. "There's real excitement when you're trying to figure out the unknown. You can't wait to find the answer.

"I've been fortunate to get my lab up and running quickly, thanks in large part to Heritage funding. I've only been in Calgary a little over a year now, and I have a lab that many of my colleagues in the US would never have had starting out."

Dr. Rebekah DeVinney is a Heritage Medical Scholar and an Assistant Professor in the Department of Microbiology and Infectious Diseases, Faculty of Medicine, University of Calgary. Her research is also supported by the Canada Foundation for Innovation and the Canadian Institutes of Health Research.

Recent publications

DeVinney R, Puente JL, Gauthier A, Goosney D, Finlay BB. Enterohaemorrhagic and enteropathogenic *Escherichia coli* use a different Tir-based mechanism for pedestal formation. *Molecular Microbiology* 2001; 41(6):1445-1458.

Gruenheid S, DeVinney R, Bladt F, Goosney D, Gelkop S, Gish GD, Pawson T, Finlay BB. Enteropathogenic *E. coli* Tir binds Nck to initiate actin pedestal formation in host cells. *Nature Cell Biology* 2001; 3(9):856-859.

Although Dr. DeVinney is in the early stages of her scientific career, she is already a pioneer in this area.

RIGHT: DR. REBEKAH DEVINNEY

Treating elbow

Yet even with the best of medical care, almost every person who suffers a traumatic elbow injury—such as a dislocation or severe fracture—will lose some range of motion in the joint, says Dr. Kevin Hildebrand, Assistant Professor in the Department of Surgery at the University of Calgary. As a matter of fact, regaining the full range of motion is extremely rare, and about 5% of severe elbow-injury patients will lose virtually all motion in the joint. This is particularly significant since, as Dr. Hildebrand points out, "the elbow's function is to position the hand in space, and if you can't move your elbow adequately, your hand movements suffer." There are also long-term implications. Parts of the joint capsule tissue will sometimes change into bone, for example. Elbow joint contracture can also lead to chronic forms of arthritis, including joint degeneration and growth of unwanted "osteophytes" (bone spurs) around the edges of the joints.

Dr. Hildebrand, who as a clinician specializes in treating elbow and wrist disorders, says it is crucial to get an elbow joint moving within a week or two after injury. "Immobilizing an injured joint makes the motion loss after an injury a lot worse." Within four to six weeks of the injury, he applies mechanical braces that "stretch" the elbow joint tissue, in an effort to push the elbow straighter or allow it to bend farther.

When physical therapies aren't effective in restoring at least functional motion, he performs a surgical procedure on the joint capsule, the many-plied tissue which envelops the elbow joint. Removing the entire joint capsule can restore some of the lost motion. In some cases, removing only part of the joint capsule, by means of arthoscopic surgery, is sufficient to release tension on the tissue. Patients who have this surgery typically regain about half of the lost motion in their elbow joint.

"My idea would be to try to find some complementary or additional non-surgical measures that we could apply to people who have just experienced this injury," Dr. Hildebrand says.

His medical research focuses on understanding the processes that cause joint contracture after traumatic injury. Dr. Hildebrand is comparing joint tissue collected from his surgical patients with normal tissue obtained from organ donors who had full motion in their uninjured elbows. He's especially interested in how the number and function of certain cells, called "myofibroblasts," compare in injured versus healthy joint tissue. An increase in myofibroblasts has been observed in fibrotic diseases, where tissues become stiff and less flexible, Dr. Hildebrand notes. Such disorders include lung fibrosis, liver cirrhosis, and such musculoskeletal conditions as Dupuytren's contracture.

Myofibroblast cells produce contractile proteins of the type normally seen in such smooth-muscle cells as those that line blood vessels. Dr. Hildebrand suspects that "somehow, the interaction between

[myofibroblast] cells and the material outside the cells in the joint capsule leads to loss of compliance in the tissue, and stiffness. So the joint can't stretch out as far as it normally would."

He has found that levels of the contractile protein "smooth-muscle actin", which is produced by myofibroblasts, are higher in injured tissue than in the control group of normal tissue. "My hypothesis is that the patients I've done surgery on have more of these myofibroblasts in their joint capsules than the tissue donors who didn't have elbow injuries or any loss of elbow motion."

If Dr. Hildebrand can show that myofibroblasts do cause or contribute to joint contracture, it would open the door to more effective and preventative treatments. In the future it might be possible, by administering a molecularly designed drug—either at the time of an injury or even several months later—to "instruct" the myofibroblast cells to stop reproducing or to stop producing the tissue-contracting proteins. Cells, however, make up only about 5% of the joint capsule tissue. So Dr. Hildebrand also plans to investigate post-injury changes in the tissue's surrounding non-cellular matrix, made up mostly of water and the protein collagen.

Almost every person who suffers a traumatic elbow injury–such as a dislocation or severe fracture–will lose some range of motion in the joint.

Another important aspect of his research is to develop an animal model of joint contracture. "If Dr. Hildebrand can develop a model of these conditions and define the mechanisms that cause the joint stiffness, he will almost certainly be able to define some very important new therapies for our patients," says Dr. Cy Frank, Head of the Orthopaedics division at the University of Calgary, and a Heritage Scientist.

Dr. Hildebrand did his residency training in Calgary with Dr. Frank, followed by a post-doctoral fellowship at the University of Pittsburgh, where he worked with Dr. Savio L.-Y. Woo on ligament healing. He then went on to St. Joseph's Hospital in London, Ontario, where Dr. Graham King encouraged him to specialize in elbow and wrist disorders.

Dr. Hildebrand is a Heritage Clinical Investigator. He has also received funding from the Canadian Orthopaedic Foundation and the University of Calgary.

Selected publications

Hildebrand KA. Patterson SD, Regan WD, MacDermid JC, King GJW. Functional outcome of semiconstrained total elbow arthroplasty. *Journal of Bone and Joint Surgery (Am.)* 2000; 82(10):1379-1386.

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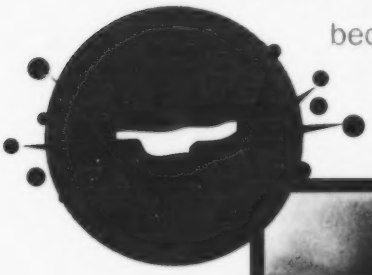
Hildebrand KA, Zhang M, van Snellenberg W, King GJW, Hart DA. Alpha-smooth muscle actin levels are elevated in human elbow joint capsules following trauma. *Journal of Orthopaedic Research*. In press.

DR. KEVIN HILDEBRAND

Growing le

Dr. William Brook learned a fascinating thing about *Drosophila*, the common fruit fly, when he took a course in developmental biology as an undergraduate student. If a *Drosophila*'s leg was cut in half, the fly would naturally regenerate the missing half of the leg. By learning more about how *Drosophila* regrows severed legs, he wondered, could medical researchers better understand how, in the course of normal development, a relatively simple cluster of cells grows to become a complex, functional limb?



"My number one interest is to understand the fundamental processes of cell pattern formation in the limbs."

DR. WILLIAM BROOK

For his doctorate in genetics at the University of Alberta's Department of Biological Sciences, Dr. Brook searched for the genes that were expressed ("switched on") in cells that regenerate the fly's limb. He recalls with a smile how his thesis supervisor, Dr. Michael Russell, now Professor Emeritus, "let me make lots of mistakes. Failure is a great teacher."

At the University of Calgary, where he has worked for the last four years, Dr. Brook continues to focus on the molecular mechanisms involved in limb development. Using fruit-fly limb and wing tissue, he studies "how simple embryonic cells turn into complicated adult structures, and what are the steps involved in that process."

Drosophila has been a favourite model since the early 1900s for investigating what Dr. Brook calls the "nuts and bolts" of development. "The fly has turned out to be a bit of a Rosetta Stone for development," he notes. "So many of the really fundamental cellular and genetic rules that govern development of the fly also govern development in higher organisms—including humans."

In 1999, the sequenced genome for *Drosophila's* 14,000 genes was published—one of the first completed genetic codes for any living organism. This advance gave developmental biologists a powerful road map for pinpointing specific genes that control development. Many of the genes and proteins

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and other developmental wonders

Many of the cellular pathways that control limb development in *Drosophila* also play a role in some potentially fatal human diseases.

involved in forming *Drosophila's* limbs are the same genes and proteins identified in limb development in such vertebrates as mice and chicken.

For example, a protein called "hedgehog" (named after a hairy mutant embryo form of *Drosophila*) switches on a gene called "dpp." The hedgehog protein and the dpp gene are both involved in cell communication and the generation of patterns during limb development "essentially anywhere you have vertebrate limbs," Dr. Brook says.

Many of the cellular pathways that control limb development in *Drosophila* also play a role in some potentially fatal human diseases. The hedgehog protein's receptor gene, called "patched", is also found in a mutant form in basal-cell carcinomas. Cell signalling by another gene, called "wingless" in flies and "WNT" in humans, is defective in many colon and breast cancers.

"My number one interest is to understand the fundamental processes of cell pattern formation in the limbs," Dr. Brook says. "As we study that, we're studying very important cell-signalling pathways, which can mutate to serious diseases like cancers in humans." rn

Dr. Brook is a Heritage Scholar who also receives funding from the Canadian Institutes of Health Research and the National Cancer Institute. He is an Assistant Professor in the Department of Biochemistry and Molecular Biology at the University of Calgary.

Selected publications

Svendsen PC, Marshall SDG, Kyba M, Brook WJ. The combgap locus encodes a zinc-finger protein that regulates cubitus interruptus during limb development in *Drosophila* melanogaster. *Development* 2000; 127(19):4083-4093.

Brook WJ, Cohen SM. Antagonistic interactions between wingless and decapentaplegic responsible for dorsal-ventral pattern in the *Drosophila* leg. *Science* 1996; 273(5280): 1373-1377.

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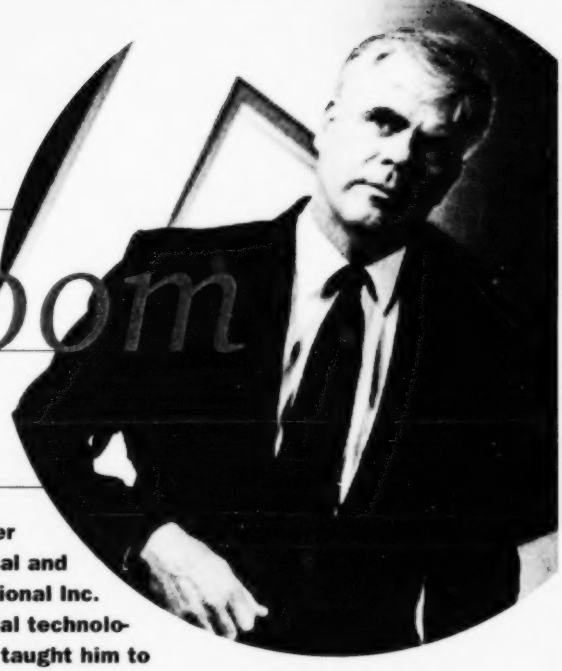
Brook WJ, Diaz-Benjumea FJ, Cohen SM. Organizing spatial pattern in limb development. *Annual Reviews: Cell Developmental Biology* 1996; 12(1):161-180.

From lab to boardroom with UTI



Sometimes, Ron Matheson feels like a kid in a candy store. Other times, he could just tear his hair out. His job, as Manager, Medical and Life Sciences, at Calgary-based University Technologies International Inc. (UTI), is focused on helping researchers commercialize biomedical technologies. Years of experience in technology commercialization have taught him to temper enthusiasm with patience.

"There's a wealth of research at the University of Calgary and the other research institutions we work with at UTI," says Matheson. "Scientists want to figure out how things work—and they've been incredibly successful at doing so. But just because you've figured out how something works and therefore have a 'target' for a potential drug, it does not mean you have a drug.

"At the University of Calgary alone we probably have more targets than a huge pharmaceutical company. The frustration and the excitement for someone like me is that we need to go much further than identifying targets, to developing the actual drugs."

After more than 20 years in the pharmaceutical industry, Matheson joined UTI in September 2000. He became a member of UTI's strong team of professionals with the mandate to move technology from an academic to a business environment. The company is wholly owned by the University of Calgary, but has a customer base that extends beyond the University. Gross revenue from licensing and sales is about $4 million Canadian annually.

"You always have to anticipate your next step. Venture capitalists and potential strategic alliance partners don't make snap decisions."

"Coming to UTI has been a great opportunity for me," says Matheson. "I enjoy early-stage product development. One of my strengths is being able to take an idea, assess it, and package a product appropriately."

What makes a good idea? It's not just something that works, notes Matheson. "Competitive positioning is critical. You have to find out what else is on the market. Are there similar products? We won't take on me-too products. We need something that can carve a niche for itself.

"To do my job well, I have to be tuned in to what's going on. I have a broad background and a good idea of what's out there, especially in gastrointestinal, cardiovascular, infectious diseases, neuroscience, and cancer—five therapeutic areas in which researchers at the University of Calgary are particularly strong."

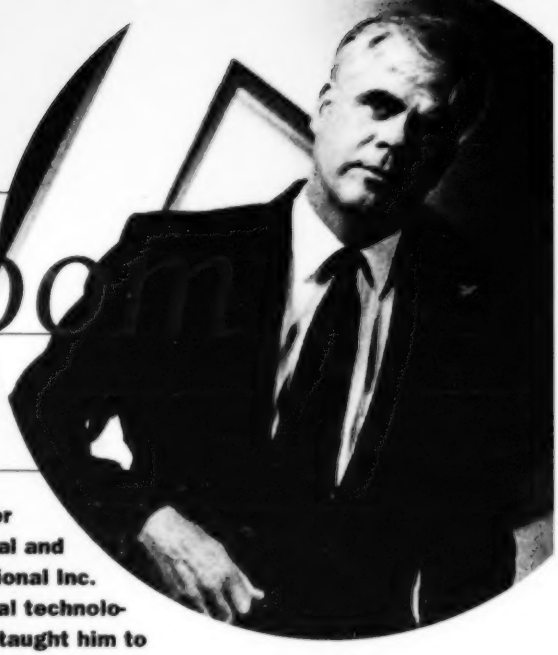
UTI handles about 30 biomedical technology disclosures per year. Once the initial technology assessment is complete and UTI takes on the technology for development, Matheson works closely with the scientific team. "A lot of technologies wouldn't be successful if you tried to license them as is," he says. "They need to be more focused. A broad technology may have five different applications. Perhaps only one has commercial potential.

"One of the toughest things is to say to people that we're not going to invest in patenting all five, only one. This information can be difficult for inventors to accept. But a patent costs about $100,000. We have to be selective about which technologies we protect."

UTI is known for its expertise in licensing, having licensed more than 360 technologies since its inception in 1989. In recent years, it has become increas-

ABOVE: RON MATHESON

From lab to boardroom with UTI



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ABOVE: RON MATHESON

ingly involved in developing spin-out companies.

In these cases, Matheson usually plays a significant role in company management, often working as the company Chief Operating Officer in the early stages. "And it's more than me—a whole team at UTI gets involved in the spin-out companies we develop. For example, Wendy Porter (UTI's Financial Administrator) will work as accountant, Oleh Hnatiuk (UTI's CEO) will chair the board.

"We work together to incubate the company, using relatively small amounts of cash from sources such as AHFMR or early-stage investors. AHFMR has been a good partner in the seed financing area, as well as for help in accessing various kinds of business expertise."

Money is always an issue for spin-out companies. Seed funding must be followed by longer-term financing from either venture capital or a public offering. "At this point, we'll be looking to put a permanent management in place," says Matheson. "The key is a well-done business plan. If the plan is solid, there's a road map to follow.

"You always have to anticipate your next step. Venture capitalists and potential strategic alliance partners don't make snap decisions. All this takes time. We are about to close a $3.5 million financing for one start-up company. It has taken about a year already. You have to start telling your story early."

Patience is truly a virtue in technology commercialization. The enthusiasm of someone like Ron Matheson behind your TC project can make the waiting easier to handle.

Commercial success starts in the lab

Great technology, excellent competitive positioning... you might think that's enough for successful commercialization of biomedical technology. Definitely not, says Ron Matheson, Manager, Medical and Life Sciences, at University Technologies International Inc. He notes that things done in the lab during technology development can be the difference between commercial success or failure. Paying attention in the early stages of technology development can have big pay-offs down the road.

Use validated models in experiments. These are tests that have been developed and validated through an open consensus process so it can be presumed that they will generate the same data at any laboratory using the same standard protocol. "Often we see that scientists haven't used validated models in their experiments," says Matheson. "It's not enough to have the method accepted by a scientific journal. Investors aren't interested unless they see something that the U.S. Food and Drug Administration will accept."

Put Good Laboratory Practices in place. These regulations are process-oriented and address matters such as organization and personnel, facilities, equipment, facility operations, test and control articles, and study protocol and conduct. "Good Laboratory Practices require a level of documentation and attention to detail that is not always present in university labs," notes Matheson. "Licensing partners and venture capitalists know that unless these procedures are followed, the data can't be used for approvals."

Pay attention to the technologies used to develop your own technology. One of the most pressing issues for many research programs is the "freedom to operate" in a world of interwoven claims to intellectual property rights. Developers may face difficulties because of the legal hurdles involved in acquiring the rights to use proprietary technologies or materials. "For example, if you use a commercial system like a gene expression system to develop your own technology, you may not have the freedom to use it commercially," says Matheson. "As a result, your innovation cannot be commercialized."

Pause before publishing. "Here's what we'd love to have happen," says Matheson. "Scientists do tests on validated models, patent the technology, and we do a license or start-up company before the results are published," says Matheson. "Of course, that would take about two years. Can you imagine me asking scientists to delay publishing that for two years? They'd think I was insane. So we end up patenting early in order to protect technologies. As a result, we patent more than we need to. Probably about half of the patents we spend money on obtaining are not ultimately useful. My advice? If you think there's commercial potential, seek expert advice before publishing."

Make a commitment. In the development of a spin-out company, the scientist needs to make a commitment, not necessarily to becoming a CEO, but certainly to becoming a CTO (chief technology officer). Says Matheson: "If this isn't going to happen, we can work around it, but the situation isn't ideal.

"The scientist/entrepreneur must be a very, very good communicator, able to create an understanding of the technology, as well as generate excitement for the technology. Even the best product has to be sold well."

The oldest person who ever lived was Jeanne Louise Calment. She was 121 years old when she died in France in 1996. Reaching 100 years old or more may still be an anomaly, but thanks to innovative medical technology, more people are reaching an advanced old age. With a higher level of education, better health habits, and increased financial security, Baby Boomers are expected to live even longer than past generations.

"I've seen newspaper articles on people who want to replicate themselves–for example, a millionaire who will pay almost any amount to clone himself in the mistaken belief that he will live forever," says University of Calgary geriatrician Dr. David Hogan, a respected expert in the area of aging. Except for a misguided few, the greatest concerns for most people as they grow older, says Hogan, are maintaining a good quality of life and independence as long as possible. "With today's advanced technologies we can extend life an inordinate amount, but the person could be a vegetable lying in a hospital bed for weeks, months, or even years. Most people would not want to live that way."

ABOVE: DR. DAVID HOGAN

They lived through the Vietnam War,

women burning their bras in the fight for equal rights, and witnessed the first man walking on the moon. The generation that extolled the line "don't trust anyone over 30" is now well over that limit itself. The first of the 6 million Baby Boomers in Canada are just turning 55 years old; in 10 short years, they will reach retirement age. Over the next 20 years, these "aging hipsters" will be accessing government and healthcare services in droves. It's a fact that's garnering a lot of attention, but some say not enough. What will happen when one third of our country's population become senior citizens? Are we prepared for the onslaught?

Moral questions abound on the issue of extending life. Some have asked how medical professionals can justify spending huge amounts of healthcare dollars to keep someone who is severely ill alive longer when the mortality rate of children in developing countries could be dramatically lowered by simple medical interventions. Should we be spending millions of dollars on healthcare services to aid our greying population at the expense of social and economic strain on younger generations? Policy-makers will have to struggle with this question, as the country's population is fast growing older. "How do you strike a balance between those who have made an investment in their country and those who will make an investment in their country?" asks Hogan who with other Canadian researchers is hoping to initiate a longitudinal study on aging in Canada. If their proposal is successful, they'll follow a group of seniors over two or more decades to see how they age and how their health changes.

Quality care = Quality of life

Quality of life is the underlying theme of Dr. Donna Wilson's study of the use of long-term-care facilities by seniors.

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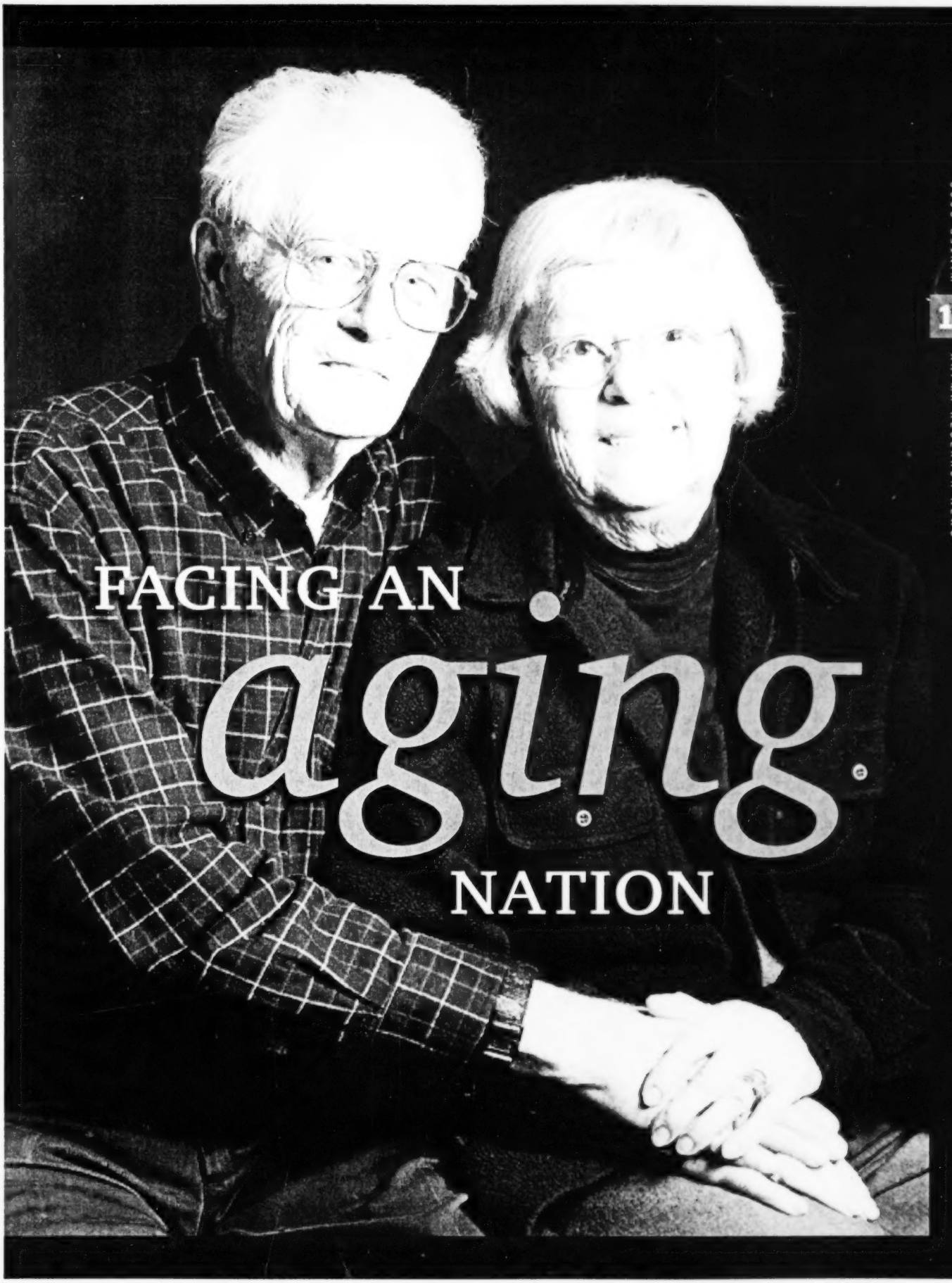
FACING AN
aging
NATION

The greatest concerns for most people as they grow older, says Hogan, are maintaining a good quality of life and independence as long as possible.

Her attempt to describe people who live in long-term care has met with some difficulty. "There is surprisingly little data on our aging population," says the University of Alberta researcher and practising registered nurse. "This is a real concern, because if they are the oldest and sickest among us, we should know the most about them. They are, instead, a missing population." What little information Dr. Wilson found before her study began showed the average nursing-home resident to be a woman in her eighties who lives in long-term care for three to four years before dying.

With her two-year Health Research Fund study, Dr. Wilson is hoping to put a face to the aged among us. She's examining 12 years of data on people who have lived and died in long-term care or who are still living there. The information is part of a massive database collected by Alberta Health and Wellness, and the largest part the government department has ever released to a researcher. "It's very exciting information because it's allowing us to look at 12 snapshots in time of about 13,000 people," she says.

Among the data she's analyzing, Dr. Wilson is looking at how often residents saw a doctor, how many times they ended up in hospital, how many times they were in outpatient or day-surgery clinics, and how often they received home care before they went into long-term care. The number crunching is all in an effort to compare how many healthcare services residents used before they were admitted, to how many they used once they entered long-term care. These figures will then be compared to similar data collected on seniors who receive home care, and on the well elderly—seniors who don't receive home care and who don't live in long-term care.

The picture already being painted by the data of elderly Albertans' use of healthcare services has surprised even Dr. Wilson: more and more of these seniors are living longer in the community before they enter long-term care, and they are sicker when they do get admitted. The average age of admittance to long-term-care facilities is now 86. While they tend to use healthcare services consistently before they are admitted, their use of healthcare services drops dramatically once they go into long-term care. "An argument could be made that admitting people into long-term care facilities actually provides them with better care," Dr. Wilson comments. "They get three healthy meals a day, help with walking, regular nursing and physician care, and more attention paid to their medications."

Most surprising, of all three groups studied, long-term care residents cost the healthcare system the least. "The only exception is that they see their doctors more frequently than home-care users and the well elderly," she notes. At 19%, the well elderly are the highest users of hospitals, followed by home-care users at 17%, and long-term-care residents at 14%. People receiving home care tend to be the most ill and unstable of the groups, stuck in a revolving door of home care, hospital stays, and irregular physician visits. "These results make you wonder if there are too few resources out there," Dr. Wilson says. "Do we have adequate levels of qualified staff to care for residents? Are there enough long-term beds out there?"

Quality of life is the underlying theme of Dr. Donna Wilson's study of the use of long-term care facilities by seniors.

"ARE THE HOME-CARE SERVICES WE OFFER SUFFICIENT?"

What can be done to prepare for the greying of the nation?

Particular communities with particular needs

"Alberta is a favoured retirement destination for senior Canadians—the taxes are cheap and the politics more in tune with their values," says Dr. Hogan. "Young people come here to work and after making their home here, often move their parents closer to them."

His University of Calgary colleague, gerontologist Dr. Daniel Lai, is looking at how Chinese seniors in Calgary are coping with aging and how their families are coping as caregivers. "When we look at caregiving in this community, the myth is that Chinese seniors are well cared for by the younger generation," he explains. "The fact is that between work, social activities, and raising their children, adult children in the Chinese community are having a tough time balancing their own lives. Throw aging parents into the mix and it gets really complicated."

Dr. Daniel Lai is looking at how Chinese seniors in Calgary are coping with aging and how their families are coping as caregivers.

Dr. Lai is looking at three questions in his two-year Health Research Fund study: how Chinese seniors access healthcare services, how their children balance the needs of their aging parents with those of their own families, and how Calgary healthcare providers can better serve the needs of this particular senior population.

A volunteer opportunity in a long-term-care facility 10 years ago led Dr. Lai, who is himself Chinese, to his current research focus. He visited a Chinese senior who spoke only Chinese and was the only Chinese person in an entire nursing unit. "It can be an incredibly isolating experience for people to be separated from their families and culture," he says. "I talk to them and play music they are familiar with to give them a connection to the outside world."

Dr. Lai hopes that his study will shed light on the lack of diversity in the resident population of long-term-care facilities, as well as the lack of understanding of multicultural health issues in the Alberta healthcare system, issues ranging from cultural sensitivity to language barriers. The impending onslaught of aging Baby Boomers may push this concern forward on the agenda.

"With the number of immigrants that have come to Canada over the last several decades, our Baby Boomer population is even more culturally diverse," he says. "Shortly, that will be reflected in our senior population. The particular needs and characteristics of seniors of various cultural backgrounds is an issue that will need to be addressed."

The continuum of care

Top Alberta researchers are addressing other major health concerns among the province's seniors. The University of Calgary's Dr. Colleen Maxwell heads a study evaluating a powerful care-needs assessment tool for Alberta's continuing-care system. This innovative tool will help community-based caregivers ensure that elderly patients are taking their medications properly, and will flag potential problem areas and instantly generate a care plan when they aren't, to avoid re-hospitalizations or complications. The study began last year in the Calgary and Chinook health regions.

In other community-based healthcare research, Dr. Lesley Brown is conducting a two-year project on age-related changes in balance, to examine whether most serious

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Preventing falls

Dr. Lesley Brown is examining whether most serious falls are preventable, and whether worrying about falling actually makes seniors more susceptible to doing so.

Dr. Brown is comparing older adults—ranging in age from 60 to 90—with a group of young, active university students to see how a threat to balance changes the way they control their balance. The two groups are being put through a series of physical tests, ranging from walking on a balance beam to standing at the edge of a raised platform, to assess their reactions.

The University of Lethbridge researcher's work has so far shown that the rigid posture people assume when there is a chance they'll fall, as well as hyper-awareness induced by fear of falling, may actually contribute to falls. Her findings could well be incorporated into rehabilitation programs for falls.

Dr. Hogan, too, has recently completed a study on fall prevention in the senior population. Nearly one third of seniors have one or more falls a year. It's a frequent cause of hospital admission, and also the most common cause of accidental or traumatic death in the elderly. His study looked at ways in which seniors over 65 who live on their own could be helped to accident-proof their homes. He's also involved in a series of studies on dementia, looking at whether the use of new medication is associated with a decreased reliance on the healthcare system, studying people at risk for dementia, and investigating interventions to prevent the condition's occurrence.

Assessing the needs of seniors

Alberta is fortunate to have some of the world's top scientists working hard to produce groundbreaking discoveries in the areas of biomedical and health research. What happens to the abundant evidence they and other scientists produce?

It's the task of AHFMR's Health Technology Assessment Unit, in collaboration with government, health authorities, and researchers at universities, to assess the benefits and risks of drugs, equipment and devices, and other health technologies being used in Alberta's healthcare system. Assessments are conducted on a request-only basis and provide objective information to guide healthcare decision-makers and patients alike.

Among the reviews the Unit has conducted are several related to Alberta's seniors. An assessment of intraocular lens implants for cataracts prompted Alberta Health and Wellness to add foldable lens implantation to the list of procedures it funds. "This change gives the elderly a choice in terms of costs and the lens they opt for," says Christa Harstall, the HTA Unit's Associate Director. "The appropriate lens used still depends on the health of the person's eyes and the expertise of their ophthalmologist."

Another therapy to undergo Unit review is a new drug treatment for age-related macular degeneration (AMD), the leading cause of blindness in Canadians over the age of 50. Ocular photodynamic therapy uses a laser-activated drug called Visudyne to treat the "wet" form of AMD, which accounts for 90% of all cases of legal blindness in these patients. Again, as a result of this HTA review, Alberta Health and Wellness will now fund the procedure.

Other HTA assessments include a review of the effectiveness of a Type II diabetes education program to help patients better manage the disease, which generally shows up later in life. The review led the Capital Health Authority to restructure its existing program. A recent HTA review of the appropriate screening interval for breast cancer in women over 50 confirmed that the guidelines produced by the Alberta Medical Association's Clinical Practice Guidelines Program were consistent with the published research. ●

ABOVE: DR. LESLEY BROWN • RIGHT: CHRISTA HARSTALL

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Confronting the future

Will we be ready for the future when it comes to our aging population? Dr. Hogan doesn't think so. "We have two decades before the aging of our population becomes a real issue. We still have time to prepare for this onslaught, but I don't get the feeling that we are doing so with any urgency. I suspect we'll just muddle through until we have a crisis in 20 years' time," he predicts.

What can be done to prepare for the greying of the nation? Dr. Hogan has some suggestions: "We need to plan strategically for healthcare service and delivery, establish teams of experts in aging, and provide them with the critical infrastructure they need to research this complex issue," he says. "It's a national issue. The federal government needs to take a lead role in this area and involve the provinces. We all have to be open to innovative changes in the way we conduct research and the way we fund it."

What's the difference between a geriatrician and a gerontologist? A geriatrician is a medical doctor with a specialty in geriatric medicine. A gerontologist is an epidemiologist or social worker with a focus on older adults living in society and how aging affects them in this broader context.

Dr. David Hogan is a geriatrician and Professor of Geriatric Medicine, in the Faculty of Medicine at the University of Calgary. Dr. Hogan has received funding for his work through the Health Research Fund, administered by the Alberta Heritage Foundation for Medical Research on behalf of Alberta Health and Wellness. He receives additional funding from the Institute of Health Economics.

Recent publications

Wolfson C, Wolfson DB, Asgharain M, M'Lan CE, Ostbye T, Rockwood K, Hogan DB. A re-evaluation of the duration of survival of the onset of dementia. *New England Journal of Medicine* 2001; 344:11-16.

Hogan DB, MacDonald FA, Betts J. A randomized controlled trial of a community-based falls consultation team. *Canadian Medical Association Journal* 2001; 165:537-43.

Dr. Donna Wilson's work is supported by the Health Research Fund administered by the Alberta Heritage Foundation for Medical Research on behalf of Alberta Health and Wellness. She is an Associate Professor in the Faculty of Nursing at the University of Alberta. She receives additional funding from the Canadian Institutes of Health Research.

Recent publications

Wilson DM, Truman CD. Addressing myths about end-of-life care: a research investigation of the use of acute-care hospitals over the last five years of life. *Journal of Palliative Care*. In press.

Wilson DM, Northcott HC, Truman CD, Smith S, Anderson M, Fainsinger R, Stingl M. Dying and death in Canada: twentieth-century location of death trends. *Evaluation and the Health Professions*. In press.

Dr. Daniel Lai's work is supported by the Health Research Fund, administered by the Alberta Heritage Foundation for Medical Research on behalf of Alberta Health and Wellness. He is an Associate Professor in the Faculty of Social Work at the University of Calgary. He receives additional funding from the Social Sciences and Humanities Research Council.

Recent publications

Lai, DWL. Use of senior center services of the elderly Chinese immigrants. *Journal of Gerontological Social Work* 2001; 35(2): 59-79.

Lai, DWL. Measuring depression of the elderly Chinese in Canada: Use of a community screening instrument. *Canadian Journal of Psychiatry* 2000; 45(3): 279-284.

Dr. Colleen Maxwell is an AHFMR Population Health Investigator. She also receives funding from the Institute for Health Economics, The Merck Company Foundation, and the Calgary and Chinook health regions.

Recent publications

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Dr. Lesley Brown's work is supported by the Health Research Fund administered by the Alberta Heritage Foundation for Medical Research on behalf of Alberta Health and Wellness. She is an Assistant Professor in the Department of Kinesiology and Physical Education at the University of Lethbridge.

Selected publications

Rankin JK, Woollacott MH, Shumway-Cook A, Brown LA. Cognitive influence on postural stability: a neuromuscular analysis in young and older adults. *Journal of Gerontology: Medical Sciences* 2000; 55A:M112-M119.

Brown LA, Shumway-Cook A, Woollacott MH. Attentional demands and postural recovery: the effects of aging. *Journal of Gerontology: Medical Sciences* 1999; 54A:M165-171.

The word "revolutionary" is a term that AHFMR Scholar Dr. Walter Maksymowych does not toss around lightly. That is the very word he uses, however, to describe the effects of a drug called infliximab on the treatment of inflammatory joint disease.

A **bright** new world

NEW TREATMENTS FOR INFLAMMATORY JOINT DISEASE

Dr. Maksymowych has been examining the effects of infliximab on a disease called ankylosing spondylitis (AS). AS is a form of arthritis that causes inflammation of the joints and ligaments of the spine and occurs very commonly in patients with Crohn's disease. It affects 150,000 to 300,000 Canadians—mainly people in their 20s and 30s—and is three times more common in men than in women. Until recently, doctors could offer little more than physiotherapy and anti-inflammatories to people who suffered from AS. But Dr. Maksymowych points out that there is now a whole new approach to this disease because of research discoveries made in the last two to three years—many of them at the University of Alberta. His AS-related research interests follow two themes: therapeutics and genetics.

Whereas infliximab has already been used successfully for the treatment of rheumatoid arthritis, Dr. Maksymowych is conducting a program to assess its effectiveness on patients with AS. Infliximab has been found to induce remissions in 90% of AS patients and Dr. Maksymowych is examining markers of cartilage damage in patients taking the drug. "Until agents like infliximab were developed, we haven't even been able to think about the possibility of preventing structural damage or joint damage for this disease," he says. "Now we've got a whole bright new world to look forward to."

Another aspect of Dr. Maksymowych's therapeutic research involves the drug pamidronate, one of a group of drugs known as bisphosphonates. In the past, researchers focused on the use of these drugs primarily for osteoporosis, but patients receiving this drug for osteoporosis also saw an improvement in their AS symptoms. Using advanced MRI techniques to document and measure information in joints, Dr. Maksymowych and radiologist Dr. Robert Lambert examined the effects of pamidronate as they related specifically to AS. The MRI data has also been particularly useful in showing how the disease evolves. The results of a double-blind controlled study funded by the Canadian Institutes of Health Research showed that pamidronate is indeed very effective in the treatment of AS.

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"Ankylosing spondylitis is the prototypic disease of a group of diseases

ABOVE: DR. WALTER MAKSYMOWYCH

of large joints known as spondyloarthropathies, which are slightly more common than rheumatoid arthritis," says Dr. Maksymowych, explaining the importance of these findings. "It is significant because it affects people early in life, in their 20s and 30s, and it's going to be with you for four or five decades, unlike rheumatoid arthritis which begins around the time of menopause. The pharmaceutical industry has paid, essentially, no attention to this disease whatsoever. Until recently, if you failed treatment with anti-inflammatories there was really nothing else to offer—and certainly no treatments that affected disease progression."

Dr. Maksymowych expects this work will be a springboard to further studies examining how pamidronate exerts its effects and hopes there will be lessons for the development of anti-inflammatory agents for other disorders. He also highlights the discoveries surrounding pamidronate to illustrate how a clinician scientist made an observation in the clinic and went from the bedside to the bench.

On the genetic side of his research, Dr. Maksymowych is collaborating with Heritage Scientist Dr. Kevin Kane in the Department of Medical Microbiology and Immunology, trying to understand why the inflammation in AS is triggered in the first place. Within all the cells of our bodies, he explains, we have highly complex, multi-catalytic enzymes called proteasomes, which act like cellular garburators. These garburators chew up certain proteins made within cells, such as those made by viruses. Immune cells screen these bits of protein once the breakdown products have been transported to the surface of the cell. The immune cells can then recognize the breakdown products as foreign and destroy cells with viruses in them. The garburators also break down proteins that are growing old, to aid in the process of renewal and rejuve-

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Collaborating on health research

Like many modern-day health researchers, Dr. Joanne Homik wears many hats. An Assistant Clinical Professor in the University of Alberta's Division of Rheumatology, Dr. Homik teaches, sees patients, does an outreach clinic, and participates in various clinical trials. She also devotes time to the Cochrane Collaboration—a project for which she is U of A's Site Representative, and a member of the musculoskeletal review group, which reviews rheumatology and osteoporosis research.

The Cochrane Collaboration is an international voluntary organization which seeks to bring together all the results of randomized trials and studies on various health areas and condense them into meta-analyses. Participants contribute by choosing a topic and doing a systematic review of all literature on that topic. "Sometimes when smaller studies are done, the results may be inconclusive because they are not statistically significant," explains Dr. Homik. "Bringing everything together like this can strengthen the estimate of how effective the drug or intervention is." A database of randomized, controlled clinical trials is maintained and all meta-analyses are published on the Cochrane Library CD-ROM.

The University of Alberta hosted the Canadian Cochrane Symposium in November 2001, and Dr. Homik was the program chair. She has been involved with the Cochrane Collaboration since 1997 when she incorporated the analysis process into her M.Sc.

After completing her master's degree, Dr. Homik spent six months working in AHFMR's Health Technology Assessment (HTA) unit. "The HTA process is very similar to the Cochrane process, and the two communities often interact," she says. "While the Cochrane Collaboration's main thrust is to find the data and synthesize the data, HTA obtains the data in whatever form it is available and goes on to assess the applicability of that data, including such factors as economics, resources, availability, and patient population."

Most of Dr. Homik's review work centres on osteoporosis and steroid-induced osteoporosis. Along with Heritage Scholar Dr. Walter Maksymowych, she established an osteoporosis education program at the University of Alberta and is a co-investigator on several clinical trials with him, as well as with Division of Rheumatology Director, Dr. Anthony Russell. "I'm not a funded researcher and I'm not a clinician scientist," says Dr. Homik, "but I like to keep my hand in research activities."

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Most of Dr. Homik's review work centres on osteoporosis and steroid-induced osteoporosis. Along with Heritage Scholar Dr. Walter Maksymowych, she established an osteoporosis education program at the University of Alberta and is a co-investigator on several clinical trials with him, as well as with Division of Rheumatology Director, Dr. Anthony Russell. "I'm not a funded researcher and I'm not a clinician scientist," says Dr. Homik, "but I like to keep my hand in research activities."

The discoveries surrounding pamidronate illustrate how a clinician scientist made an observation in the clinic and went from the bedside to the bench.

nation. Different people have different garburators which produce different breakdown products. So when someone is exposed to salmonella, a trigger of this form of arthritis, the range of breakdown products produced by one person's garburators will be different from that of another. Dr. Maksymowych suspects that a process of molecular mimicry occurs in people who have AS, with the result that some of the bacterial proteins start to look identical to those that arise from the breakdown of the body's proteins.

Dr. Maksymowych goes on to explain that AS is almost 100% genetic. To date, however, only one of the genes involved has been identified—B-27, a very common gene. The University of Alberta is one of only two Canadian centres involved in a North American gene consortium trying to pinpoint the other genes. He points out that AS may be the first autoimmune disease to have its genetic background identified. "We are currently involved in several of the major therapeutic and genetic initiatives related to this disease internationally," he adds.

In addition to his work in the lab, Dr. Maksymowych has recently participated in the production of an educational video about AS, entitled "Attack from Within". Produced entirely at the University of Alberta and aired on Access TV, the video is an attempt to engage the research community and inform the public about research activities on this disease at the U of A.

Dr. Walter Maksymowych is an AHFMR Scholar, as well as an Associate Professor and consultant rheumatologist at the University of Alberta. He also receives support from The Arthritis Society and the Canadian Institutes of Health Research.

Recent publications

Maksymowych WP, Lambert R, Jhangri GS, LeClercq S, Chiu P, Wong B, Aaron S, Russell AS. Clinical and radiological amelioration of refractory peripheral spondyloarthritis by pulse intravenous pamidronate therapy. *Journal of Rheumatology* 2001; 28(1):144-155.

Maksymowych WP. Anti-inflammatory and immunomodulatory therapies in spondyloarthropathies. *Current Opinion in Investigational Drugs* 2000; 1(1):63-69.

Preg

Many expectant mothers are turning to complementary therapies, everything from herbal teas to nutritional supplements to homeopathic preparations. But just because something is "natural" doesn't mean it's always healthy for people—especially for pregnant women.

"I think it's important that we remember that complementary therapies can have negative as well as positive effects."

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nancy and complementary therapies

...sometimes dangerous mix

"I think it's important that we remember that complementary therapies can have negative as well as positive effects," says Dr. Maeve O'Beirne, Assistant Professor in the departments of Family Medicine and Community Health Sciences at the University of Calgary. Some popular supplements, such as valerian root (used as a sleep aid) and black cohosh (used to induce labour), can harm pregnant women and their babies. Other supplements can interact harmfully with prescription medicines; for example, garlic pills with a commonly prescribed blood thinner, heparin. On the other hand, ginger root, used as an alternative to prescription medication for treating "morning sickness" vomiting, appears to be comparatively safe and effective, says Dr. O'Beirne.

In Alberta, most healthcare providers don't know what supplements and other complementary therapies their pregnant patients are using. Dr. O'Beirne is preparing a province-wide, questionnaire-based study to collect this information.

"The idea is that once pregnant women have told us what they're using, and we've compiled the most common [therapies], then we can start doing further research to see if they actually do work and if they're safe in pregnancy."

She and her research team have completed a preliminary, small-scale study based on interviews with 24 pregnant women who said they were using some type of complementary therapy. The team has also explored the issue in focus groups with obstetricians, family physicians, and midwives. Initial data indicate discrepancies between what medical professionals thought or were told their patients were using, and the complementary therapies these pregnant women actually used.

There are a number of reasons why women don't tell their healthcare providers about complementary therapies they're using. The provider may seem too busy, or perhaps not interested in complementary therapies or knowledgeable about them. But lack of communication and knowledge can be dangerous. To cite an example from Australia, research has linked some herbal teas consumed by pregnant women to biliary atresia, a condition in the fetus where the blood vessels in the liver don't form properly.

Dr. O'Beirne plans to distribute her anonymous questionnaire to healthcare providers throughout the province, to hand out to their pregnant patients. With care providers' co-operation, she hopes to get a 30% to 50% response rate. Providers who participate will receive a report on the most common therapies being used and the information sources patients are relying on, as well as the reasons why patients aren't telling providers about their complementary therapy use.

Dr. O'Beirne, whose family practice involves mostly obstetric care, credits Dr. Wayne Elford, Professor Emeritus in the University of Calgary's Department of Family Medicine, with encouraging her to pursue research in family medicine.

Dr. O'Beirne's research project is supported by the Health Research Fund, administered by AHFMR on behalf of Alberta Health and Wellness. Her initial study received funding from the Ruth Rannie Endowment Fund and the Calgary Health Region.

Selected publications

Tudiver F, Brown JB, Medved W, Herbert C, Ritvo P, Guibert R, Haggerty J, Goel V, Smith P, O'Beirne M, Katz A, Moliner P, Ciampi A, Williams JI. Making decisions about cancer screening when the guidelines are unclear or conflicting. *Journal of Family Practice* 2001; 50(8):682-687.

Verhoef MJ, Hilsden RJ, O'Beirne M. Complementary therapies and cancer care: an overview. *Patient Education and Counseling* 1999; 38(2):93-100.

Of mice and malaria

Each year, 200 to 300 million people are infected with malaria, and approximately 2 million of them die of the mosquito-transmitted disease. The World Health Organization estimates that malaria kills 1 child every 30 seconds. Most of these children live in sub-Saharan Africa, but the reach of the disease is spreading—such factors as the El Niño weather phenomenon and other climatic events, economic activity or agricultural policy that changes land-use practices, and mass movement of refugees can all affect mosquito-breeding sites.

AHFMR student Bryan Yipp is enrolled in the Leaders in Medicine program at the University of Calgary and is working toward a combined M.D. and M.Sc. degree in Medical Sciences and Immunology. In the lab of Heritage Senior Scholar Dr. May Ho, Bryan studies the molecular mechanisms of disease in the infection caused by the deadliest of the four parasites that cause malaria in humans–*Plasmodium falciparum*.

Bryan explains that when the *P. falciparum* parasite infects a red blood cell, it grows to maturity inside the cell and starts to produce its own proteins. These proteins eventually get exported to the outside surface of the infected red blood cell and enable that cell to cling to blood vessels. This process is called cytoadherence and is one of the unique features that make this parasite so deadly. "This whole process basically removes the parasite from the circulation so it can avoid being filtered out by the spleen," Bryan says. "This increases the parasite's chance of surviving in the host. It also leads to the demise of the human host by causing obstruction in the circulation, leading in turn to low oxygen levels in the tissues, metabolic disturbances, and multi-organ failure."

A large portion of Bryan's project is focused on establishing the first-ever *in vivo* model of this

Bryan studies the molecular mechanisms of disease in the infection caused by the deadliest of the four parasites that cause malaria in humans—*Plasmodium falciparum*.

process to study the adhesion molecules in cytoadherence. Mouse models have proved ineffective in the past, as *P. falciparum* cannot invade mouse red blood cells and mouse parasites behave differently than the human species. Bryan's lab uses a model created by grafting human skin onto SCID mice–mice that do not have an immune system to reject the graft. When the graft heals, infected red blood cells are injected into the skin graft, where the adhesion process in blood vessels can be observed with a microscope.

This model also provides an excellent means of evaluating possible treatments to inhibit the cytoadherence process. Working in conjunction with researchers at the Laboratory for Parasitic Diseases, National Institutes of Health, Bryan and his colleagues are testing the anti-adhesive effect of a peptide called y179. They have found that the peptide not only successfully inhibited the infected red blood cells from adhering to blood vessels, but could also reverse cytoadherence that has already occurred. In other words, in a patient already exhibiting symptoms of malaria, this peptide could potentially detach the infected red blood cells and reverse the disease's symptoms.

A large portion of Bryan's project is focused on establishing the first ever *in vivo* model of this process to study the adhesion molecules in cytoadherence.

Bryan plans to continue evaluating other potential anti-adhesive treatments for malaria using the SCID mouse model–a model he admits is difficult to work with. "The skin grafts are delicate and the procedure requires considerable surgical skill," he points out. "But it is a unique and powerful tool."

Bryan Yipp holds an Alberta Heritage Foundation for Medical Research Studentship and is enrolled in the University of Calgary's Leaders in Medicine program.

Selected publication

Yipp BG, Anand S, Schollaardt T, Patel KD, Looareesuwan S, Ho M. Synergism of multiple adhesion molecules in mediating cytoadherence of *Plasmodium falciparum*-infected erythrocytes to microvascular endothelial cells under flow. *Blood* 2000; 96(6):2292-2298.

PHOTOS: BRYAN YIPP

reader resources

Research views

Dalhousie University Health Law Institute
http://is.dal.ca/~wwwlaw/hli/

Rebekah DeVinney

Dr. Rebekah DeVinney's web page
http://www.med.ucalgary.ca/webs/bprg/Rdevinney.html

Treating elbow disorders

University of Calgary Division of Orthopedic Surgery
http://www.acs.ucalgary.ca/~ortho/

Growing legs and other developmental wonders

Dr. William Brook's web page
http://www.ucalgary.ca/~brook/

From lab to boardroom with UTI

University Technologies International Inc.
http://www.uti.ca

The aging nation

National Center for Injury Prevention and Control
http://www.cdc.gov/ncipc/factsheets/fallcost.htm

Health Canada Aging and Seniors
http://www.hc-sc.gc.ca/seniors-aines/

University of Alberta Faculty of Nursing
http://www.nursing.ualberta.ca/homepage.nsf/website

Dr. Lesley Brown's web page
http://home.uleth.ca/~l.brown

A bright new world: new treatments for inflammatory joint disease

Spondylitis Association of America
www.spondylitis.org

Collaborating on health research

The Cochrane Collaboration
http://www.cochrane.org

Assessing the needs of seniors

AHFMR Health Technology Assessment Unit
http://www.ahfmr.ab.ca/hta/

Pregnancy and complementary therapies: a sometimes dangerous mix

Motherisk
Phone: (416) 813-6780
http:// www.motherisk.org

Of mice and malaria

Malaria Foundation International
http://www.malaria.org/

Jacob Jaremko – 2001-2002 McLeod Scholarship winner

Dr. Ron Zernicke's web page
http://www.kin.ucalgary.ca/HPL/html/zernicke.html

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reader resources

Dalhousie University Health Law Institute
http://is.dal.ca/~wwwlaw/hli/

Dr. Lesley Brown's web page
http://home.uleth.ca/~l.brown

Dr. Rebekah DeVinney's web page
http://www.med.ucalgary.ca/webs/bprg/Rdevinney.html

Spondylitis Association of America
www.spondylitis.org

University of Calgary Division of Orthopedic Surgery
http://www.acs.ucalgary.ca/~ortho/

The Cochrane Collaboration
http://www.cochrane.org

Dr. William Brook's web page
http://www.ucalgary.ca/~brook/

AHFMR Health Technology Assessment Unit
http://www.ahfmr.ab.ca/hta/

University Technologies International Inc.
http://www.uti.ca

Motherisk
Phone: (416) 813-6780
http:// www.motherisk.org

National Center for Injury Prevention and Control
http://www.cdc.gov/ncipc/factsheets/fallcost.htm

Malaria Foundation International
http://www.malaria.org/

Health Canada Aging and Seniors
http://www.hc-sc.gc.ca/seniors-aines/

University of Alberta Faculty of Nursing
http://www.nursing.ualberta.ca/homepage.nsf/website

Dr. Ron Zernicke's web page
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Jacob Jaremko – McLeod Scholarship winner

Jacob Jaremko went into medicine because of one of his little sisters.

The winner of the 2001-2002 Lionel E. McLeod Health Research Scholarship says that when his sister was diagnosed with diabetes, it made him realize he wanted to help people. Midway through his studies in Civil Engineering at the time, Jacob realized that if he continued as a pure engineer he would be "ignoring the passage of life".

"It was very frustrating for my whole family when my sister was diagnosed," he explains. "I realized that there are more important things, like when people get sick, and that through medicine I could do something to make more of a difference." His very first research interest–working on an artificial pancreas–allowed Jacob to apply engineering principles directly to diabetes.

A native Calgarian, Jacob began his combined degree program in 1997, working toward an M.D. as well as a Ph.D. in biomedical engineering through the University of Calgary's Faculty of Medicine. When shopping around for a Ph.D. project, he became interested in adolescent idiopathic scoliosis, a spinal deformity which affects more than 94,000 children in Canada between the ages of 11 and 14. Cancer risk is associated with the spinal x-rays currently used to monitor progression of the disease. Jacob is now working on developing a non-invasive means of detecting spinal curve through scanning the surface of the torso with low-power lasers which generate a three-dimensional image of the existing spinal deformity. He is involved in a multi-disciplinary, multi-centre collaboration involving research teams in Calgary and Montreal. More knowledge in this area could lead to earlier detection of the disease, a reduction of radiation exposure for patients, and improved design of braces for scoliosis patients.

Jacob is currently finishing off his thesis, and after another year and a half of medical school he plans to do a clinical residency in either orthopedics or radiology. In the latter years of his residency, he hopes to get back into bioengineering-related research.

The Lionel E. McLeod Health Research Scholarship is awarded annually by AHFMR to an outstanding student at the University of Alberta, Calgary, or British Columbia for research related to human health. Dr. McLeod was the founding president of AHFMR from 1981 to 1990 and was Head of Endocrinology at the University of Alberta, Dean of Medicine at the University of Calgary, and President and Chief Executive Officer of the University Hospital, Vancouver.

Jacob Jaremko is an MD/PhD student at the University of Calgary working in the lab of Dean of Kinesiology Dr. Ronald Zernicke. In addition to the McLeod Scholarship, Jacob also holds a Canadian Institutes of Health Research MD/PhD Studentship.

Selected publications

Jaremko J, Rorstad O. Advances toward the implantable artificial pancreas for treatment of diabetes. *Diabetes Care* 1998; 21(3):444-450.

Jaremko J, Delorme S, Dansereau J, Labelle H, Ronsky J, Poncet P, Harder J, Dewar R, Zernicke RF. Use of neural networks to correlate spine and rib deformity in scoliosis. *Computer Methods in Biomechanics and Biomedical Engineering* 2000; 3(3):203-213.

Jaremko JL, Poncet P, Ronsky J, Harder J, Dansereau J, Labelle H, Zernicke RF. Estimation of spinal deformity in scoliosis from torso surface cross sections. *Spine* 2001; 26(14):1583-1591.

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Physicians: please place in your patient waiting rooms.

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